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(21) International Application Number: PCT/US98/25892 (22) International Filing Date: 8 December 1998 (08.12.98) (30) Priority Data: 60/067,888 8 December 1997 (08.12.97) US 60/082,663 22 April 1998 (22.04.98) US 60/108,536 16 November 1998 (16.11.98) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications US 60/067,888 (CIP) Filed on 8 December 1997 (08.12.97) US 60/082,663 (CIP) Filed on 22 April 1998 (22.04.98) US 60/108,536 (CIP) Filed on 16 November 1998 (16.11.98) (71) Applicant (for all designated States except US): BETH ISRAEL DEACONESS MEDICAL CENTER [US/US]; 330 Brookline Avenue, Boston, MA 02215 (US).		(72) Inventor; and (75) Inventor/Applicant (for US only): SUKHATME, Vikas, P. [US/US]; 36 Sky View Circle, Newton Center, MA 02159 (US). (74) Agents: HOGLE, Doreen, M. et al.; Hamilton, Brook, Smith & Reynolds, P.C., Two Militia Drive, Lexington, MA 02421 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>	
(54) Title: METHODS OF PRODUCING ANTI-ANGIOGENIC PROTEINS: ENDOSTATIN, ANGIOSTATIN OR RESTIN, USING A PICHIA YEAST EXPRESSION SYSTEM (57) Abstract Methods for making proteins with anti-angiogenic properties are disclosed, including angiostatin, endostatin and restin. The system used is a yeast expression system which produces biologically active proteins at high titer, specifically the <i>Pichia pastores</i> yeast expression system.			

EXHIBIT**D**

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